GB2171302A

Publication Title:

No title available

Abstract:

Abstract not available for GB2171302A Data supplied from the esp@cenet database - Worldwide

---

(12) UK Patent Application (19) GB (11) 2 171 302 A

(43) Application published 28 Aug 1986

(21) Application No 8527159

(22) Date of filing 4 Nov 1985

(30) Priority data

(31) 668200 (32) 5 Nov 1984 (33) US
723565 15 Apr 1985

(51) INT CL[4]
A61K 31/195

(52) Domestic classification (Edition H):
A5B 20X 20Y H J
U1S 1313 2410 2415 A5B

(56) Documents cited
GB 1399887 GB 1246141

(58) Field of search
A5B
Selected US specifications from IPC sub-class A61K

(71) Applicant
Dr Wilhelm Hoerrmann,
Staltacherstrasse 34, D-8127 Iffeldorf, Federal Republic of Germany

(72) Inventor
Dr Wilhelm Hoerrmann

(74) Agent and/or Address for Service
Robert J. Cummings, 6 High Stobhill, Morpeth, Northumberland NE61 2TT

ERRATUM

SPECIFICATION NO. 2171302A

Page 1, Line 51 *for* L cis– *read* L–4–cis–
Page 1, Line 92 *for* 0,003/0,03g read 0,003–0,03g
Page 1, Line 98 *for* cis hydroxy–L– *read* cis–4–hydroxy–L–
Page 1, Line 100 *for* cis hydroxy–L– *read* cis–4–hydroxy–L–
Page 1, Line 104 *for* cis hydroxy–L–proline *read* cis–4–hydroxy–L–proline
Page 1, Line 107 *for* cis hydroxy–L– *read* cis–4–hydroxy–L–
Page 1, Line 110 *for* cis hydroxy–L– *read* cis–4–hydroxy–L–
Page 1, Line 112 *after* cis *insert* –4–
Page 1, Line 113 *for* hydroxy–L proline *read* hydroxy–L–proline
Page 1, Line 115 *for* 0,003-0,3g/kg *read* 0,003–0,03g/kg
Page 2, Line 13 *for* 0.003 to 0.3 *read* 0.003 to 0.03
Page 2, Line 38 *for* cis–4–hydroxy/L– *read* cis–4–hydroxy–L–
Page 2, Line 49 *for* 0.003 to 0.3 *read* 0.003 to 0.03

THE PATENT OFFICE
1 October 1986

A

(12) UK Patent Application (19) GB (11) 2 171 302 A

(43) Application published 28 Aug 1986

(21) Application No 8527159

(22) Date of filing 4 Nov 1985

(30) Priority data

(31) 668200 (32) 5 Nov 1984 (33) US
723565 15 Apr 1985

(51) INT CL[4]
A61K 31/195

(52) Domestic classification (Edition H):
A5B 20X 20Y H J
U1S 1313 2410 2415 A5B

(56) Documents cited
GB 1399887 GB 1246141

(58) Field of search
A5B
Selected US specifications from IPC sub-class A61K

(71) Applicant
Dr Wilhelm Hoerrmann,
Staltacherstrasse 34, D-8127 Iffeldorf, Federal Republic of Germany

(72) Inventor
Dr Wilhelm Hoerrmann

(74) Agent and/or Address for Service
Robert J. Cummings, 6 High Stobhill, Morpeth, Northumberland NE61 2TT

(54) Therapeutic hydroxyprolines

(57) Cis-4-hydroxy-L-proline or cis-3-hydroxy-L-proline are used in the treatment of carcinomas, diseases of the blood vessels and viral diseases. The hydroxyproline is administered intravenously as a solution or orally in tablets or dragees either with or without the other amino acids proline, valine, alanine, lysine, hydroxylysine and glycine. The hydroxyproline or the other amino acids can be in free form or in acetylated form or as peptides.

GB 2 171 302 A

SPECIFICATION

Tumor therapy

The main subject of this application is a new therapy for cancer especially carcinomas and related tumors. The expression "related tumors" means tumors which are like carcinomas of an embryologically epithelial origin. Examples are astrocytomas, neurinomas, suprarenal (medulla) tumors and so on.

In the years 1933 - 1946 Helen M. Dyer of the United States National Cancer Institute administered a wide range of amino acids in experimental tumors of the mouse. Among others she mentioned hydroxyproline, but it is known that results of experimental animal tumors are scarcely transferable to human cancer.

In the last about 20 years electronmicroscopic device have shown the existence of the so called cytoskeleton within the cells. Immunological methods applied on the cytoskeleton are today used to recognize the origin of a cancer in their metastases. Applicant's concept, however, goes farther and postulates that a disturbance of the cytoskeleton is an essential factor for the pathogenesis of cancer, especially carcinomas. When in cancer cells and tissues the cytoskeleton, the cell junctions, the basal laminas and the filaments of the extra-cellular matrix, the connective tissues additionally are out of order it is doubtless indicated to substitute the constituents of these filamental systems which are specific amino acids.

From this point of view one of the most important of these amino acids is hydroxyproline. Here, however, it is not sufficient to differentiate between L and D configuration as Dyer had done. The decisive act is to differentiate also between cis and trans isomers of hydroxyproline which arises of the asymmetrical nature of the hydroxyl-group bearing carbon atom (this carbon atom is preferably number 4, but also number 3 is to be considered).

The proof that that is so was established by tests which were performed according to applicant's suggestion. These were not tests on experimental animal tumors which are scarcely transferable in their results to native human cancer. They were performed in human cell culture, the cells of which were removed from brain tumor patient by neurosurgery. The administering of L cis - Hydroxyproline to these astrocytoma tumor cells brought about not only a considerably slowed rate of cell division but also induced morphological redifferentiation, that is the cells resembled no longer tumor but normal astroglial cells. On the other side the trans isomer of L-4-Hydroxyproline showed not at all any positive effects.

Hydroxyproline may be given alone or combined with other amino acids which are occuring in the above named filamental system as there are proline, valine, alanine, lysine, hydroxylysine, glycine, cysteine and cystine.

The administration of such compounds however is not restricted to cancer cases alone, but is also indicated in cases of viral infection and blood vessels disease. Even neurological and rheumatological indications are marking out.

The administering of amino acids in their free form is a possible method. Their specific effect however can also be brought into existence by administering compounds containing these amino acids that is for examples in acetylated form or as corresponding peptides. That means the administering of the named amino acids can be directly or indirectly.

Amino acids are scarcely toxic at all, therefore the named compounds have a wide doses range. However as with all amino acids therapy the known contraindications should wherever possible be excluded, especially patients with renal diseases.

The therapeutic administering of these compounds is principally the same as with all amino acid therapy. Tabletts or dragees for oral, solutions for intravenous (or central intravenous) administering. Dosis range for hydroxyproline is 0,01 - 0,1 g daily (in severe cases up to 0,2 g daily) per kg of the patient's body weight. Dosis range for hydroxyproline combined with proline, valine, alanine, lysine, hydroxylysine and glycine is for hydroxyproline 0,006 - 0,06 g and 0,003 / 0,03 g for each of the other amino acid, per kg of the patient's body weight, daily.

CLAIMS

1. A medicament containing cis hdyroxy - L - proline

2. A medicament containing cis hydroxy - L - proline in combination with proline, valine, alanine, lysine, hydroxylysine and glycine.

3. A method of treating carcinomas and related tumors by administering cis hydroxy - L - proline 0,01 - 0,2 g/kg daily.

4. A method of treating bloodvessels diseases by administering cis hydroxy - L - proline 0,01 - 0,2 g/kg daily.

5. A method of treating viral diseases by administering cis hydroxy - L - proline 0,01 - 0,2 g/kg daily.

6. The methods of claims 3, 4 and 5 where cis hydroxy-L proline 0,006 - 0,06 is combined with proline, valine, alanine, lysine, hydroxylysine and glycine 0,003 - 0,3 g/kg of each.

7. Cis-4-hydroxy-L-proline for use in a method for the treatment of the human body by therapy.

8. Cis-3-hydroxy-L-proline for use in a method for the treatment of the human body by therapy.

9. The compound claimed in Claim 1 or Claim 2 in a medicament comprising also the amino acids proline, valine, alanine, lysine, hydroxylysine and glycine.

10. Use of the compound as claimed in Claim 7 or 8, in the preparation of a medicament for the treatment of carcinomas or related tumours.

11. Use of the compound as claimed in Claim 7 or 8 in the preparation of a medicament for the treatment of diseases of the blood vessels.

12. Use of the compound as claimed in Claim 7

or 8 in the preparation of a medicament for the treatment of viral diseases.

13. Use of the compound as claimed in Claim 10, 11 or 12 in which the medicament also contains the amino acids proline, valine, alanine, lysine, hydroxylysine and glycine.

14. Use of the compound as claimed in Claim 10, 11 or 12 in which the daily dose is 0.01 to 0.2 gramme per kilogramme of the patient's body weight.

15. Use of the compound as claimed in Claim 13 in which the daily dose is 0.006 to 0.06 gramme of the hydroxyproline and 0.003 to 0.3 gramme of each of the additional amino acids per kilogramme of the patient's body weight.

New claims or amendments to claims filed on 6 May 1986

New or amended claims:- 1 to 13

1. Use of cis-4-hydroxy-L-proline in the preparation of a medicament for the treatment of carcinomas or related tumours.

2. Use of cis-4-hydroxy-L-proline in the preparation of a medicament for the treatment of diseases of the blood vessels.

3. Use of cis-4-hydroxy-L-proline in the preparation of a medicament for the treatment of viral diseases.

4. Use of cis-4-hydroxy-L-proline in the preparation of a medicament for the treatment of neurological conditions.

5. Use of cis-4-hydroxy-L-proline in the preparation of a medicament for the treatment of rheumatological conditions.

6. The preparation of a medicament as claimed in any preceding claim using cis-3-hydroxy-L-proline instead of cis-4-hydroxy/ L-proline.

7. The preparation of a medicament according to any preceding claim, the medicament also comprising the amino acids proline, valine, alanine, lysine, hydroxylysine, glycine, cysteine and cystine.

8. The preparation of a medicament according to any claim of claims 1 to 6 in which the daily dose is 0.01 to 0.2 gramme per kilogramme of the patient's body weight.

9. The preparation of a medicament according to claim 7, in which the daily dose is 0.006 to 0.06 gramme of the hydroxyproline and 0.003 to 0.3 gramme of each of the additional amino acids per kilogramme of the patient's body weight.

10. The preparation of a medicament according to any preceding claim, in which the hydroxyproline or the other amino acids when present are each in the form of a derived compound.

11. A medicament made by the preparation according to any preceding claim.

12. A medicament according to claim 11, substantially as herein described.

13. The preparation according to any claim of claims 1 to 10 substantially as herein described.

Printed in the UK for HMSO, D8818935, 7/86, 7102.
Published by The Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from which copies may be obtained.